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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/791,033	KELLY-AEHLE, SANDRA	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 22-34* is/are pending in the application.

4a) Of the above claim(s) *7,8 and 11-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10 and 22-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/19/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of species D is acknowledged. The traversal is on the grounds that the groups of claims are not separate because the strains are all known in the art. This is not found persuasive because the basis for the distinct species is not whether the strains are known in the art but rather the basis for restriction is that the groups are drawn to the different properties for each bacterium, such as divergent mutations, and mutations that affect different genes and enzymes. Thus, each bacterial species performs its function based on different mutations, thus the bacteria are structurally and functionally divergent. Each gene has a separate and distinct structure and function, thus each group has a different mode of operation and function within the *Salmonella*.

It is the examiner's position that even though the groups share the same class number, the search is still extremely burdensome. The distinct inventions require a search for each species of enteropathogenic bacteria which is not coextensive. There is search burden also in the non-patent literature since the bacterial strain of interest may be in journal articles devoted solely to a particular strain which would not have described the other strains. Searching, therefore is not coextensive. As such, it would be burdensome to search all of the species together. Therefore, restriction for examination purposes as indicated is proper and is therefore made FINAL.

Amendment Entry

2. The amendment filed March 2, 2006 has been entered. Claim 1 has been amended. Claims 17-21 have been cancelled. Claims 7-8 and 11-16 have been withdrawn from consideration. Claims 1-6, 9-10 and 22-34 are under consideration in this office action.

Specification

3. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The benefit of the earlier filing date under 35 U.S.C. 120 of the parent application Serial No. 09/122,299 has been denied for claims 9-10 for the instant application. The claims in the instant continuation-in-part application recites a feature, i.e. the method wherein the enteropathogenic bacteria is a derivative of a pathogenic strain of bacteria characterized by: a) a lack of a functioning native chromosomal gene encoding a first enzyme which is a B-aspartic semialdehyde dehydrogenase (Asd); b) the presence of a first recombinant gene encoding a second Asd enzyme wherein the first recombinant gene cannot recombine to replace the defective chromosomal gene; c) the presence of a second recombinant gene encoding a desired polypeptide; and d) physical linkage

between the first recombinant gene and the second recombinant gene, wherein loss of the first recombinant gene causes the bacteria to lyse when in an environment which requires expression of the first recombinant gene for cell survival, or wherein the enteropathogenic bacteria are selected from the group of strains consisting of χ6097 (ATCC 67537), χ3520 (ATCC 53681), χ4072 (ATCC 67538), χ3008 (ATCC 53680), χ2108 (ATCC 53678), and χ6097 (ATCC 67813) which was not disclosed or adequately supported by a proper disclosure under 35 U.S.C. 112 in the parent application. This feature has been first introduced and adequately supported in the instant continuation-in-part application and thus such claims are entitled only to the filing date of the instant application; *In re Von Lagenhoven*, 458 F.2d 132, 136, 173 USPQ 426, 429 (CCPA 1972) and *Chromalloy American Corp. v. Alloy Surfaces Co., Inc* ., 339 F. Supp. 859, 874, 173 USPQ 295, 306 (D. Del. 1972).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-6 and 23-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtiss, III et al., (1996) in view of Peterson (4,449,968).

The claims are drawn to a method of delivering a protein to a domestic bird comprising administering to the bird in a whole-body spray an effective amount of a live

avirulent derivative of an enteropathogenic bacterium comprising a recombinant gene that codes for the expression of the protein, wherein (a) the enteropathogenic bacterium is other than one that causes respiratory disease in birds, (b) the protein is delivered to the bird, and (c) the spray is composed of droplets having a mean diameter of 40-200 microns.

Curtiss III et al., (1996) teach recombinant avirulent *Salmonella* vaccines for poultry. Numerous *Salmonella* serotypes are capable of infecting young chicks and the younger the chick the greater the susceptibility to infection (page 365). *Salmonella* can lead to a dose dependant transient lymphocyte depletion in the bursa of Fabricius and spleen with an induced impairment in immune responsiveness and enhancement in establishing a Salmonella carrier state (page 365-366). The objective was to minimize colonization of the intestinal tract and shedding by diverse *Salmonella* serotypes (page 366). The prior art teaches inoculation of avirulent Salmonella as live oral vaccines (page 366). A genetically altered avirulent *Salmonella typhimurium* vaccine strain for immunizing chicks and young pellets has been designed and constructed by the authors (page 366). The live avirulent recombinant vaccine strains when used for oral immunization attach to, invade and colonize the gut-associated lymphoid tissue (GALT) where they continue to synthesize the foreign colonization or virulence antigen for several days to a few weeks (page 369). Curtiss III et al., teaches the use of avirulent Salmonella as antigen delivery vector. In the system developed, the attenuated Salmonella vaccine strain has a chromosomal *Δasd* mutation eliminating the synthesis of B-aspartic semialdehyde dehydrogenase. The authors have constructed plasmid cloning vectors using the wild-type *asd* gene from either *S. mutans* or from *S. typhimurium* to complement the chromosomal *Δasd* mutation (page 369). The loss of

the Asd+ plasmid causes DAPless death and cell lysis with release of foreign antigens (page 370). These deletion mutations were generated by transposon mutagenesis (page 366). Single immunization used 10^7 colony-forming units, (CFU) to induce protection to challenges (page 367). Immunization of chicks occurred on day-of-hatch, 3 days of age and 1, 2, 3, 4 and 14-20 weeks of ages with comparisons of single versus multiple immunizations and with doses ranging from 10^6 to 10^9 CFU (page 367). Young chicks immunized with one or two doses of the avirulent strain displayed a reduced ability to be colonized in the intestinal tract by virulent *S. typhimurium* strains (page 367). The avirulent *S. typhimurium* vaccine strain was administered as a coarse spray to newly hatched chicks and then administered in the drinking water to chicks 10 days of age or older (page 370). For chicks destined to become breeders or layers, a booster immunization should be administered at 14-18 weeks of age dependent on husbandry considerations (page 370). An anticipated immunization regime would be to vaccinate breeders with the live avirulent strain followed by vaccination by coarse spray or in drinking water of the chicks from those breeders (page 370). Finally, infection with wild type virulent *Salmonella* can cause lymphocyte depletion with an impairment in immune responsiveness, thus the authors anticipate that birds hatched from eggs from immunized breeders and then immunized should display a more robust immune response and thus have a performance advantage over chicks that have never been immunized (page 371). Curtiss III et al., has been discussed above, however Curtiss III et al., does not teach using a coarse spray with specific droplet diameters.

Peterson teaches dosing the vaccine in a spray and spraying downward onto the chicks (col. 1, lines 47-50). Most of the spray droplets are of a size large enough to fall onto the chicks substantially without remaining airborne long enough to be inhaled by the chicks (col. 1, lines 50-53). Some of the droplets come to rest on other parts of the

upper body portions of the chicks and the natural movements of the chicks tend to spread the droplets to the eyes of the chicks and to adjacent chicks (col. 1, lines 57-61). Furthermore, the chicks are inclined to peak at the droplets so the vaccine is received through the mouth of the chick (col. 1-2, lines 65-6). The poultry vaccination system can administer live vaccines to the chicks without handling each chick (col. 2, lines 20-22). The vaccine spray nozzles in combination with air pressure result in a large percentage of the vaccine being dispersed in droplets with diameter between 90 microns to 150 microns (col.6, lines 40-43). The aerosol spray reliably administers vaccine to baby chicks without individual handling that prevents harm and without overdosing (col. 2, lines 18-27). Similar methods of administration are known in the art but several may cause damage to the chicks or require time consuming techniques: de-beaking and eye dropper inoculations require the handling of each chick; spraying into the mouth may result in secondary infections and even death; and inhaling the vaccine resulted in chick lung diseases and sometimes death (col. 1, lines 20-40).

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the method of Curtiss III, to use a poultry vaccination system as taught by Peterson since only routine skill would have been required to disperse droplets of 90-190 microns. One would have a reasonable expectation of success since only routine skill would be required to vaccinate the birds in a poultry vaccination system. Moreover no more than routine skill would have been required when Curtiss III, already teach using a coarse spray to orally deliver a vaccine for enteropathogenic bacterium while Peterson teach a preference that the spray droplets are large enough to fall onto the birds without remaining airborne long enough to be inhaled.

6. Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtiss, III et al., (1996) and Peterson (US Patent 4,449,968) further in view of Curtiss, III (US Patent 5,672,345).

The claims are drawn to a method of delivering a protein to a domestic bird wherein the enteropathogenic bacteria is a derivative of a pathogenic strain of bacteria characterized by: a) a lack of a functioning native chromosomal gene encoding a first enzyme which is a B-aspartic semialdehyde dehydrogenase (Asd); b) the presence of a first recombinant gene encoding a second Asd enzyme wherein the first recombinant gene cannot recombine to replace the defective chromosomal gene; c) the presence of a second recombinant gene encoding a desired polypeptide; and d) physical linkage between the first recombinant gene and the second recombinant gene, wherein loss of the first recombinant gene causes the bacteria to lyse when in an environment which requires expression of the first recombinant gene for cell survival, or wherein the enteropathogenic bacteria are selected from the group of strains consisting of χ6097 (ATCC 67537), χ3520 (ATCC 53681), χ4072 (ATCC 67538), χ3008 (ATCC 53680), χ2108 (ATCC 53678), and χ6097 (ATCC 67813). Curtiss III (1996) and Peterson have been discussed above, however neither teach the specific derivative of the pathogenic strain of bacteria.

Curtiss, III teach materials and methodologies for preparing vaccines and recombinant DNA expression products to genetically engineered microorganisms which are useful to express desired gene products because they balance lethals which can be maintained in a genetically stable population (col. 1, lines 20-25). The invention

teaches maintaining a desired recombinant gene comprising growing genetically engineered cells characterized by: a) a lack of a functioning native chromosomal gene encoding a first enzyme, which is essential for cell survival, wherein the first enzyme catalyzes a step in the biosynthesis of an essential cell wall structural component; b) the presence of a first recombinant gene encoding an second enzyme which is a functional replacement for the first enzyme, wherein said first recombinant gene cannot replace the defective chromosomal gene; c) the presence of a second recombinant gene encoding a desired polypeptide; and d) physical linkage between the first recombinant gene and the second recombinant gene, wherein loss of the first recombinant gene causes the cells to lyse when the cells are in an environment where a product due to the expression of the first recombinant gene is absent (col. 4, lines 35-53). The invention teach that there is a mutation in a gene encoding B-aspartic semialdehyde dehydrogenase (Asd) (col. 5, lines 1-4). The patent states that a deposit of the cultures was made to ATCC, wherein the deposits are χ6097 (ATCC 67537), χ3520 (ATCC 53681), χ4072 (ATCC 67538), χ3008 (ATCC 53680), χ2108 (ATCC 53678), and χ6097 (ATCC 67813) (col. 23, lines 15-25). Thus, these deposited strains are the same instantly claimed deposits, to thereby meet the limitations of the claims. The cells of the invention are useful for commercial production of desired products, for components of vaccines for immunizing individuals, and for release into the environment. An "individual" treated with a vaccine of the invention is defined herein as including mammals, and various species of birds, including domestic birds, just as required by the claims (col. 7, lines 57-61). Administration of a live vaccine of the type

disclosed above to an animal may be by any known or standard technique (col. 21, lines 20-21). These include oral ingestion, gastric intubation, broncho-nasal spraying or in forms of aerosols (col. 20, lines 43-46). All of these methods allow the live vaccine to easily reach the GALT or BALT cells and induce antibody formation (col. 21, lines 26-29).

Therefore, it would have been prima facie obvious at the time of applicants' invention to modify the method of Curtiss III et al., and Peterson, to use the enteropathogenic bacteria are selected from the instantly claimed group as taught by Curtis, III since only routine skill would have been required to exchange the enteropathogenic bacteria comprising the recited gene when the prior art already teach the *asd* gene's usefulness for delivering proteins to domestic birds. One would have a reasonable expectation of success since only routine skill would be required to vaccinate the birds using a well known gene and strains of bacteria known in the art to be capable of delivery proteins. Moreover no more than routine skill would have been required when Curtiss III et al., already teach using a coarse spray to orally deliver a vaccine for enteropathogenic bacterium while Curtis, III teach administration via oral ingestion or by aerosol spray when aerosol and oral vaccination is a well known and popular technique to deliver birds droplets within the instantly claimed ranges.

Double Patenting

7. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re*

Ockert, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

8. Claims 1-6 and 22-33 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-6 and 12-23 of prior U.S. Patent No. 6,866,847. This is a double patenting rejection because the claims are identical.

Prior Art

9. Curtiss III, et al., (1990) teach the stabilization of recombinant avirulent vaccine strain wherein the gene for B-aspartic semialdehyde dehydrogenase (Asd+) from Streptococcus mutans was present in plasmid vectors to complement an *Δasd* mutation in the chromosome of the *Salmonella* vaccine strain. Table 1 teaches the source of bacterial strains χ6097, χ3520 and χ4072. Grieve teaches the wide usage of for the administration of live vaccines to poultry by spray.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ja-Na Hines
June 6, 2006

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
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